General

Guideline Title

Headaches: diagnosis and management of headaches in young people and adults.

Bibliographic Source(s)

National Clinical Guideline Centre. Headaches: diagnosis and management of headaches in young people and adults. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Sep. 38 p. (Clinical guideline; no. 150).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Clinical Excellence (NICE) (see the "Availability of Companion Documents" field for the full version of this guidance).

Assessment

Evaluate people who present with headache and any of the following features, and consider the need for further investigations and/or referral*:

- Worsening headache with fever
- Sudden-onset headache reaching maximum intensity within 5 minutes
- New-onset neurological deficit
- New-onset cognitive dysfunction
- Change in personality
- Impaired level of consciousness
- Recent (typically within the past 3 months) head trauma
- Headache triggered by cough, valsalva (trying to breathe out with nose and mouth blocked) or sneeze
- Headache triggered by exercise
- Orthostatic headache (headache that changes with posture)
- Symptoms suggestive of giant cell arteritis
- Symptoms and signs of acute narrow-angle glaucoma
- A substantial change in the characteristics of their headache

Consider further investigations and/or referral for people who present with new-onset headache and any of the following:

- Compromised immunity, caused, for example, by human immunodeficiency virus (HIV) or immunosuppressive drugs
- Age under 20 years and a history of malignancy
- A history of malignancy known to metastasise to the brain
- Vomiting without other obvious cause

Consider using a headache diary to aid the diagnosis of primary headaches.

If a headache diary is used, ask the person to record the following for a minimum of 8 weeks:

- Frequency, duration and severity of headaches
- Any associated symptoms
- All prescribed and over the counter medications taken to relieve headaches
- Possible precipitants
- Relationship of headaches to menstruation

Diagnosis

Tension-Type Headache, Migraine (With or Without Aura) and Cluster Headache

Diagnose tension-type headache, migraine or cluster headache according to the headache features in the table.

Table: Diagnosis of Tension-Type Headache, Migraine and Cluster Headache

Headache Feature	Tension-Type Headache	Migraine (With or Without Aura)	Cluster Headache
Pain location[1]	Bilateral	Unilateral or bilateral	Unilateral (around the eye, above the eye and along the side of the head/face)
Pain quality	Pressing/tightening (nonpulsating)	Pulsating (throbbing or banging in young people aged 12–17 years)	Variable (can be sharp, boring, burning, throbbing or tightening)
Pain intensity	Mild or moderate	Moderate or severe	Severe or very severe
Effect on activities	Not aggravated by routine activities of daily living	Aggravated by, or causes avoidance of, routine activities of daily living	Restlessness or agitation
Other symptoms	None	Unusual sensitivity to light and/or sound or nausea and/or vomiting Aura[2] Symptoms can occur with or without headache and: • Are fully reversible • Develop over at least 5 minutes • Last 5−60 minutes Typical aura symptoms include visual symptoms such as flickering lights, spots or lines and/or partial loss of vision; sensory symptoms such as numbness and/or pins and needles; and/or speech disturbance.	On the same side as the headache: • Red and/or watery eye • Nasal congestion and/or runny nose • Swollen eyelid • Forehead and facial sweating • Constricted pupil and/or drooping eyelid
Duration of	30 minutes–continuous	4–72 hours in adults	15–180 minutes

Headache Feature	Tension-Type Headache		Migraine (With or Without Aura)		Cluster Headache	
Frequency of headache	<15 days per month	≥15 days per month for more than 3 months	<15 days per month	≥15 days per month for more than 3 months	1 every other day to 8 per day[3], with remission[4] >1 month	1 every other day to 8 per day[3], with a continuous remission[4] <1 month in a 12-month period
Diagnosis	Episodic tension-type headache	Chronic tension-type headache[5]	Episodic migraine (with or without aura)	Chronic migraine[6] (with or without aura)	Episodic cluster headache	Chronic cluster headache

[1] Headache pain can be felt in the head, face or neck.

[2] See the recommendations below for further information on diagnosis of migraine with aura.

[3] The frequency of recurrent headaches during a cluster headache bout.

[4] The pain-free period between cluster headache bouts.

[5] Chronic migraine and chronic tension-type headache commonly overlap. If there are any features of migraine, diagnose chronic migraine.

[6] NICE has developed technology appraisal guidance on Botulinum toxin type A for the prevention of headaches in adults with chronic migraine (headaches on at least 15 days per month of which at least 8 days are with migraine).

Migraine with Aura

Suspect aura in people who present with or without headache and with neurological symptoms that:

- Are fully reversible and
- Develop gradually, either alone or in succession, over at least 5 minutes and
- Last for 5–60 minutes

Diagnose migraine with aura in people who present with or without headache and with one or more of the following typical aura symptoms that meet the criteria for suspecting aura above:

- Visual symptoms that may be positive (for example, flickering lights, spots or lines) and/or negative (for example, partial loss of vision)
- Sensory symptoms that may be positive (for example, pins and needles) and/or negative (for example, numbness)
- Speech disturbance

Consider further investigations and/or referral for people who present with or without migraine headache and with any of the following atypical aura symptoms that meet the criteria for suspecting aura above:

- Motor weakness or
- Double vision or
- Visual symptoms affecting only one eye or
- Poor balance or
- Decreased level of consciousness

Menstrual-Related Migraine

Suspect menstrual-related migraine in women and girls whose migraine occurs predominantly between 2 days before and 3 days after the start of menstruation in at least 2 out of 3 consecutive menstrual cycles.

Diagnose menstrual-related migraine using a headache diary (see the recommendations concerning headache diary in the section "Assessment" above) for at least 2 menstrual cycles.

Medication Overuse Headache

Be alert to the possibility of medication overuse headache in people whose headache developed or worsened while they were taking the following drugs for 3 months or more:

- Triptans, opioids, ergots or combination analgesic medications on 10 days per month or more or
- Paracetamol, aspirin or a non-steroidal anti-inflammatory drug (NSAID), either alone or in any combination, on 15 days per month or more

Management

All Headache Disorders

Consider using a headache diary:

- To record the frequency, duration and severity of headaches
- To monitor the effectiveness of headache interventions
- As a basis for discussion with the person about their headache disorder and its impact

Consider further investigations and/or referral if a person diagnosed with a headache disorder develops any of the features listed in the first bulleted list under "Assessment" above.

Do not refer people diagnosed with tension-type headache, migraine, cluster headache or medication overuse headache for neuroimaging solely for reassurance.

Information and Support for People With Headache Disorders

Include the following in discussions with the person with a headache disorder:

- A positive diagnosis, including an explanation of the diagnosis and reassurance that other pathology has been excluded and
- The options for management and
- Recognition that headache is a valid medical disorder that can have a significant impact on the person and their family or carers

Give the person written and oral information about headache disorders, including information about support organisations.

Explain the risk of medication overuse headache to people who are using acute treatments for their headache disorder.

Tension-Type Headache

Acute Treatment

Consider aspirin**, paracetamol or an NSAID for the acute treatment of tension-type headache, taking into account the person's preference, comorbidities and risk of adverse events.

Do not offer opioids for the acute treatment of tension-type headache.

Prophylactic Treatment

Consider a course of up to 10 sessions of acupuncture over 5–8 weeks for the prophylactic treatment of chronic tension-type headache.

Migraine With or Without Aura

Acute Treatment

Offer combination therapy with an oral triptan† and an NSAID, or an oral triptan and paracetamol, for the acute treatment of migraine, taking into account the person's preference, comorbidities and risk of adverse events. For young people aged 12–17 years consider a nasal triptan in preference to an oral triptan.

For people who prefer to take only one drug, consider monotherapy with an oral triptan†, NSAID, aspirin** (900 mg) or paracetamol for the acute treatment of migraine, taking into account the person's preference, comorbidities and risk of adverse events.

When prescribing a triptan† start with the one that has the lowest acquisition cost; if this is consistently ineffective, try one or more alternative triptans.

Consider an anti-emetic in addition to other acute treatment for migraine even in the absence of nausea and vomiting.

Do not offer ergots or opioids for the acute treatment of migraine.

For people in whom oral preparations (or nasal preparations in young people aged 12–17 years) for the acute treatment of migraine are ineffective

or not tolerated:

- Offer a non-oral preparation of metoclopramide or prochlorperazine†
- Consider adding a non-oral NSAID or triptan† if these have not been tried

Prophylactic Treatment

Discuss the benefits and risks of prophylactic treatment for migraine with the person, taking into account the person's preference, comorbidities, risk of adverse events and the impact of the headache on their quality of life.

Offer topiramate† or propranolol for the prophylactic treatment of migraine according to the person's preference, comorbidities and risk of adverse events. Advise women and girls of childbearing potential that topiramate† is associated with a risk of fetal malformations and can impair the effectiveness of hormonal contraceptives. Ensure they are offered suitable contraception.

If both topiramate† and propranolol are unsuitable or ineffective, consider a course of up to 10 sessions of acupuncture over 5–8 weeks or gabapentin† (up to 1200 mg per day) according to the person's preference, comorbidities and risk of adverse events.

For people who are already having treatment with another form of prophylaxis such as amitriptyline†, and whose migraine is well controlled, continue the current treatment as required.

Review the need for continuing migraine prophylaxis 6 months after the start of prophylactic treatment.

Advise people with migraine that riboflavin (400 mg† once a day) may be effective in reducing migraine frequency and intensity for some people.

Combined Hormonal Contraceptive Use By Women and Girls With Migraine

Do not routinely offer combined hormonal contraceptives for contraception to women and girls who have migraine with aura.

Menstrual-Related Migraine

For women and girls with predictable menstrual-related migraine that does not respond adequately to standard acute treatment, consider treatment with frovatriptan† (2.5 mg twice a day) or zolmitriptan† (2.5 mg twice or three times a day) on the days migraine is expected.

Treatment of Migraine During Pregnancy

Offer pregnant women paracetamol for the acute treatment of migraine. Consider the use of a triptan† or an NSAID after discussing the woman's need for treatment and the risks associated with the use of each medication during pregnancy.

Seek specialist advice if prophylactic treatment for migraine is needed during pregnancy.

Cluster Headache

Acute Treatment

Discuss the need for neuroimaging for people with a first bout of cluster headache with a general practitioner (GP) with a special interest in headache or a neurologist.

Offer oxygen and/or a subcutaneous† or nasal triptan† for the acute treatment of cluster headache.

When using oxygen for the acute treatment of cluster headache:

- Use 100% oxygen at a flow rate of at least 12 litres per minute with a non-rebreathing mask and a reservoir bag and
- Arrange provision of home and ambulatory oxygen

When using a subcutaneous† or nasal triptan†, ensure the person is offered an adequate supply of triptans calculated according to their history of cluster bouts, based on the manufacturer's maximum daily dose.

Do not offer paracetamol, NSAIDS, opioids, ergots or oral triptans for the acute treatment of cluster headache.

Prophylactic Treatment

Consider verapamil† for prophylactic treatment during a bout of cluster headache. If unfamiliar with its use for cluster headache, seek specialist advice before starting verapamil, including advice on electrocardiogram monitoring.

Seek specialist advice for cluster headache that does not respond to verapamil†.

Seek specialist advice if treatment for cluster headache is needed during pregnancy.

Medication Overuse Headache

Explain to people with medication overuse headache that it is treated by withdrawing overused medication.

Advise people to stop taking all overused acute headache medications for at least 1 month and to stop abruptly rather than gradually.

Advise people that headache symptoms are likely to get worse in the short term before they improve and that there may be associated withdrawal symptoms, and provide them with close follow-up and support according to their needs.

Consider prophylactic treatment for the underlying primary headache disorder in addition to withdrawal of overused medication for people with medication overuse headache.

Do not routinely offer inpatient withdrawal for medication overuse headache.

Consider specialist referral and/or inpatient withdrawal of overused medication for people who are using strong opioids, or have relevant comorbidities, or in whom previous repeated attempts at withdrawal of overused medication have been unsuccessful.

Review the diagnosis of medication overuse headache and further management 4–8 weeks after the start of withdrawal of overused medication.

Notes

*For information on referral for suspected tumours of the brain or central nervous system see Referral guidelines for suspected cancer (NICE clinical guideline 27); update under development (publication date to be confirmed).

**Because of an association with Reye's syndrome, preparations containing aspirin should not be offered to people aged under 16 years.

†At the time of publication (September 2012), the following drugs did not have a United Kingdom (UK) marketing authorisation for the indication presented in the guideline:

- Triptans (except nasal sumatriptan) in people aged under 18 years
- Prochlorperazine (except for the relief of nausea and vomiting)
- Topiramate in people under 18 years
- Gabapentin
- Amitriptyline
- Riboflavin (available as a food supplement. When advising this option, the prescriber should take relevant professional guidance into account.)
- Frovatriptan
- Zolmitriptan
- Subcutaneous triptans in people aged under 18 years
- Nasal triptans
- Verapamil

The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors and the prescribing advice provided by the Joint Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) for further information.

Clinical Algorithm(s)

The recommendations from this guideline have been incorporated into a NICE pathway.

Scope

Disease/Condition(s)

- Primary headaches, including:
  - Migraine with or without aura
  - Menstrual related migraine
  - Chronic migraine
  - Tension-type headache
  - Cluster headache
- Secondary headache from medication overuse
- More than one primary headache syndrome

Note: This guideline does not cover primary or secondary headaches other than those specified above, cranial neuralgias and facial pain, or comorbidities.

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Prevention

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Obstetrics and Gynecology

Pediatrics

Pharmacology

Preventive Medicine

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To make recommendations on the diagnosis and management of primary headache and medication overuse headache in young people (aged 12 or over) and adults

Target Population

Young people (aged 12 or over) and adults in all settings in which National Health Service (NHS) healthcare is provided, with particular consideration given to women and girls of reproductive age

Interventions and Practices Considered

Diagnosis/Assessment

1. Pain location and quality
2. Severity and duration of headache
3. Frequency of headache
4. Other symptoms
5. Effect on daily activity
6. Concomitant medications and relationship to timing of headaches
7. Frequency of reassessment
8. Neuroimaging for first bout of cluster headache

Management/Counseling/Treatment

1. Use of a headache diary
2. Additional investigation
3. Referral to a specialist if needed
4. Patient counseling and provision of written and oral information
5. Pharmacologic treatment:
    - Tension-type headache: aspirin, paracetamol or a non-steroidal anti-inflammatory drug (NSAID)
    - Migraine with or without aura:
        - Oral triptan and an NSAID or oral triptan and paracetamol (nasal triptan in place of an oral triptan for patients 12-17 years old)
        - Monotherapy with oral triptan, NSAID, aspirin or paracetamol
        - Anti-emetic therapy
        - For people for whom oral or nasal preparations are ineffective: non-oral metoclopramide or prochlorperazine and a non-oral NSAID or triptan (if not already used)
        - Combined hormonal contraceptives for contraception to women and girls who have migraine with aura should not be offered routinely
        - Frovatriptan or zolmitriptan for menstrual-related migraine
        - Paracetamol for pregnant women (also consider triptan or an NSAID)
    - Cluster headache: oxygen (ambulatory, home administration) and/or subcutaneous or nasal triptan
6. Medication overuse headache:
    - Withdrawal of medication with appropriate counseling, follow-up and support
    - Prophylaxis of primary headache
    - Specialist referral or inpatient withdrawal in selected cases
    - Follow-up and review of diagnosis

Prevention

1. Tension-type headache: acupuncture
2. Migraine with or without aura:
    - Topiramate or propranolol (with contraception for women of child-bearing capability)
    - Acupuncture or gabapentin
    - Continuation of amitriptyline if migraine is well controlled
    - Riboflavin
    - Obtaining specialist advice for prophylactic treatment of pregnant women
3. Cluster headache:
    - Verapamil

- Specialist advice for verapamil and electrocardiogram monitoring
- Specialist advice for verapamil failure

Note: The following were considered and not recommended:

Neuroimaging for tension-type headache, migraine, cluster headache or medication overuse headache solely for reassurance
Opioids for the acute treatment of tension-type headache
Ergots or opioids for the acute treatment of migraine
Paracetamol, NSAIDS, opioids, ergots or oral triptans for acute treatment of cluster headache

Major Outcomes Considered

- Response rate to treatment
- Resource use including general practitioner (GP) consultation, accident and emergency attendance, investigations and referral to secondary care
- Percentage responders with 25%, 50% and 75% reduction in baseline headache frequency
- Incidental radiological findings
- Headache response up to 2 hours after treatment
- Freedom from pain at up to 2 hours
- Sustained freedom from pain at 24 hours
- Sustained headache response at 24 hours
- Acute medication use
- Incidence of serious adverse events
- Change in patient-reported headache days, frequency and intensity
- Change in anxiety and depression
- Change in health related quality of life
- Change in headache specific quality of life
- Cost-effectiveness
- Cost–utility
- Cost-benefit
- Cost-consequence

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Clinical Excellence (NICE) (see the "Availability of Companion Documents" field for the full version of this guidance).

Searching for Evidence

Clinical Literature Search

Systematic literature searches were undertaken to identify evidence within published literature in order to answer the review questions as per The Guidelines Manual (see the "Availability of Companion Documents" field). Clinical databases were searched using relevant medical subject

headings, free-text terms and study type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English language. All searches were conducted on MEDLINE and Embase. The Cochrane Library was searched for all intervention questions. Additional subject specific databases were used for some questions: Cinahl for diaries, treatment questions and patient information; PsycINFO for education and self-management programmes, psychological therapies, medication over use headaches and patient information; AMED for non-pharmacological treatment of headaches. All searches were updated on March 13, 2012. No papers after this date were considered.

Search strategies were checked by looking at reference lists of relevant key papers, checking search strategies in other systematic reviews and asking the Guideline Development Group (GDG) for known studies. The questions, the study types applied, the databases searched and the years covered can be found in Appendix D of the full guideline document (see the "Availability of Companion Documents" field).

During the scoping stage, a search was conducted for guidelines and reports on the websites listed below and on organisations relevant to the topic. A full list of websites is included in Appendix D of the full guideline document (see the "Availability of Companion Documents" field). Searching for grey literature or unpublished literature was not undertaken. All references sent by stakeholders were considered.

- Guidelines International Network database (www.g-i-n.net)
- National Guideline Clearing House (www.guideline.gov/)
- National Institute for Health and Clinical Excellence (NICE) (www.nice.org.uk)
- National Institutes of Health Consensus Development Program (consensus.nih.gov/)
- National Library for Health (www.library.nhs.uk/).

Health Economic Literature Search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting a broad search relating to the guideline population in the National Health Service (NHS) economic evaluation database (NHS EED), the Health Economic Evaluations Database (HEED) and health technology assessment (HTA) databases with no date restrictions. Additionally, the search was run on MEDLINE, with a specific economic filter, from 2008, to ensure recent publications that had not yet been indexed by these databases were identified. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English language.

The search strategies for health economics are included in Appendix D of the full guideline document (see the "Availability of Companion Documents" field). All searches were updated on January 18, 2012. No papers published after this date were considered.

Evidence of Clinical Effectiveness

Literature Review

The process for review of evidence of effectiveness is as follows:

The Research Fellows:

- Identified potentially relevant studies for each review question from the relevant search results by reviewing titles and abstracts – full papers were then obtained.
- Reviewed full papers against pre-specified inclusion/exclusion criteria to identify studies that addressed the review question in the appropriate population and reported on outcomes of interest (review protocols are included in Appendix C of the full guideline document) (see the "Availability of Companion Documents" field), excluded studies lists are in Appendix O of the full guideline document (see the "Availability of Companion Documents" field). The excluded studies list only details studies excluded after the full papers were ordered. Many would have previously been excluded when the titles and abstracts were reviewed.
- Critically appraised relevant studies using the appropriate checklist as specified in The Guidelines Manual (see the "Availability of Companion Documents" field).
- Extracted key information about the study's methods and results into evidence tables (evidence tables are included in Appendix E of the full guideline document [see the "Availability of Companion Documents" field]).
- Generated summaries of the evidence by outcome (included in the relevant chapter write-ups) and produced evidence statements indicating the number of included studies, sample size (number randomised), direction of effect, uncertainty and Grading of Recommendations Assessment, Development and Evaluation (GRADE) quality rating:
    - Randomised studies: meta analysed, where appropriate and reported in GRADE profiles (for clinical studies)
    - Observational studies: data presented as a range of values in adapted GRADE profiles
    - Diagnostic studies: data presented as a range of values in adapted GRADE profiles

- Prognostic studies: data presented as a range of values in adapted GRADE profiles
- Qualitative studies: the quality of reporting for each study was summarised for three criteria in the guideline text: population, methods and analysis

Inclusion/Exclusion

See the review protocols in Appendix C of the full guideline document (see the "Availability of Companion Documents" field) for full details.

Note these key points:

The age range for this guideline was 12 years and over. Studies that included people younger than 12 were included only if the mean age of the population was over 12 years.

Crossover trials were only included in the review questions for acute treatment, however they were only included if it was clear from the paper that all participants included in the analysis had treated one headache attack only with each treatment, or if the data for the first crossover period only was available, in which case the study could be analysed as a parallel trial.

Placebo controlled trials were not included for the review question on the acute treatment of migraine as the GDG agreed that people seeking medical help for a migraine attack would have already tried over the counter medications. Therefore drug trials only were included if there was a head-to-head comparison.

The GDG agreed that for the majority of intervention review questions a sample size cut-off of 50 participants (25 per arm) was appropriate due to there being sufficient evidence with sample sizes greater than 50 which would provide a better estimate of the effect size. For most prognostic and diagnostic review questions, larger sample size cut-offs were applied. There were some exceptions in which lower sample size cut-offs were applied, or not cut-off values, when the GDG were aware that sufficient evidence at larger sample sizes would be lacking. These were (with reference to the chapter in the full guideline document):

- Indications for consideration of additional investigation (Chapter 4) – Minimum n=any
- Headache diaries for the diagnosis and management of primary headaches and medication overuse headache (Chapter 6) – Minimum n=any
- Imaging for diagnosis in people with suspected primary headache (Chapter 8.2) – Minimum n=any
- Imaging as a management strategy for people with suspected primary headaches (Chapter 8.3) – Minimum n=20 per arm
- Patient information and support (Chapter 9) – Minimum n=any
- Acute pharmacological treatment of cluster headache (Chapter 12) – Minimum n=any
- Prophylactic pharmacological treatment of cluster headache (Chapter 16) – Minimum n=any
- Prophylactic non-pharmacological management of primary headaches with psychological therapies (Chapter 23) – Minimum n=25 total
- Prophylactic non-pharmacological management of primary headaches with education and self-management (Chapter 26) – Minimum n=25 total

Evidence of Cost-Effectiveness

Literature Review

The Health Economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts – full papers were then obtained
- Reviewed full papers against pre-specified inclusion/exclusion criteria to identify relevant studies (see below)
- Critically appraised relevant studies using the economic evaluations checklist as specified in The Guidelines Manual (see the "Availability of Companion Documents" field)
- Extracted key information about the study's methods and results into evidence tables (evidence tables are included in Appendix E of the full guideline document [see the "Availability of Companion Documents" field]).
- Generated summaries of the evidence in NICE economic evidence profiles (included in the relevant chapter write-ups) – see the full guideline document for details.

Inclusion/Exclusion

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost–utility, cost-effectiveness, cost-benefit and cost-consequence analyses) and comparative costing studies that addressed the review question in the relevant population were considered potentially applicable as economic evidence.

Studies that only reported cost per hospital (not per person), or only reported average cost effectiveness without disaggregated costs and effects, were excluded. Abstracts, posters, reviews, letters/editorials, foreign language publications and unpublished studies were excluded. Studies judged to have an applicability rating of 'not applicable' were excluded (this included studies that took the perspective of a non-Organisation for Economic Co-operation and Development [OECD] country).

Remaining studies were prioritised for inclusion based on their relative applicability to the development of this guideline and the study limitations. For example, if a high quality, directly applicable United Kingdom (UK) analysis was available other less relevant studies may not have been included. Where exclusions occurred on this basis, this is noted in the relevant section.

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist in The Guidelines Manual (see the "Availability of Companion Documents" field) and the health economics research protocol in Appendix C of the full guideline document (see the "Availability of Companion Documents" field). When no relevant economic analysis was found from the economic literature review, relevant UK NHS unit costs related to the compared interventions were presented to the GDG to inform the possible economic implication of the recommendation to make.

Number of Source Documents

Assessment and Diagnosis

- Indications for consideration of additional investigations = 3
- Screening questionnaires for primary headache = 11
- Imaging for the diagnosis of primary headaches = 7
- Imaging as a management strategy for primary headaches = 1
- Patient diaries for diagnosis and management of primary headaches = 7

Management

- Patient information and support in headache management = 11
- Acute pharmacological treatment of tension type headache = 13
- Acute pharmacological treatment of migraine = 35
- Treatment of cluster headache = 9 acute treatment, 5 prophylactic pharmacologic treatment
- Prophylactic pharmacological treatment of tension-type headache (TTH) & migraine = 1 TTH, 21 migraine
- Non-pharmacological treatment of primary headaches = 26
- Management of medication overuse headache = 3

Management During Pregnancy and Contraceptive Use

- Management of primary headache during pregnancy = 3
- Contraception use in girls and women with migraine = 2

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in GRADE (Grading of Recommendations Assessment, Development and Evaluation)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate

Level	Description
Very Low	Any estimate of effect is very uncertain

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Clinical Excellence (NICE) (see the "Availability of Companion Documents" field for the full version of this guidance).

Methods of Combining Clinical Studies

Data Synthesis for Intervention Reviews

Available Case Analysis

Estimates of effect from individual studies were based on available case analysis (ACA) where it was possible to extract these data. ACA was defined as analysis using all participants with data available for the outcome being considered. For example, for dichotomous outcomes, the denominator is the number of participants with available data and the numerator is the number who experienced the event. Participants for whom data for that outcome were not available are assumed to be missing at random. Where ACA was not possible data were reported as in the study and this is explained in the introduction of the relevant clinical review.

Meta-Analyses

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5.1) software. Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for the binary outcomes: responder rate; resource use including general practitioner (GP) consultation, accident and emergency attendance, investigations and referral to secondary care; percentage responders with 25%, 50% and 75% reduction in baseline headache frequency; incidental radiological findings; headache response up to 2 hours; freedom from pain at up to 2 hours; sustained freedom from pain at 24 hours; sustained headache response at 24 hours; acute medication use; incidence of serious adverse events.

The continuous outcomes (change in patient-reported headache days, frequency and intensity; change in anxiety and depression [e.g. HAD]; change in health related quality of life [e.g. SF-36 or EuroQoL]; change in headache specific quality of life) were analysed using an inverse variance method for pooling weighted mean differences and where the studies had different scales, standardised mean differences were used. Final values were reported where available for continuous outcomes in preference of change scores. However, if change scores only were available, these were reported and meta-analysed with final values.

Statistical heterogeneity was assessed by considering the chi-squared test for significance at $p<0.1$ or an I-squared inconsistency statistic of >50% to indicate significant heterogeneity. Where significant heterogeneity was present, we carried out predefined subgroup analyses if possible. Subgroups were: age (12<18, or 18 and over), dose or route of administration.

Assessments of potential differences in effect between subgroups were based on the chi-squared tests for heterogeneity statistics between subgroups. If no sensitivity analysis was found to completely resolve statistical heterogeneity then a random effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect.

The means and standard deviations of continuous outcomes were required for meta-analysis. However, in cases where standard deviations were not reported, the standard error was calculated if the p-values or 95% confidence intervals were reported and meta-analysis was undertaken with the mean and standard error using the generic inverse variance method in Cochrane Review Manager (RevMan5) software. When the only evidence was based on studies which only presented means, this information was summarised in the Grading of Recommendation Assessment, Development and Evaluation (GRADE) tables without calculating the relative and absolute effect.

For binary outcomes, absolute event rates were also calculated using the GRADEpro software using event rate in the control arm of the pooled results.

Network Meta-Analyses

Network meta-analysis was conducted for the review questions on the acute and prophylactic treatment of migraine. This allowed indirect comparisons of all the drugs included in the review when no direct comparison was available. A hierarchical Bayesian network meta-analysis (NMA) was performed using the software WinBUGS. We adapted a three-arm random effects model template for the networks, from the University of Bristol website (https://www.bris.ac.uk/cobm/research/mpes/mtc.html). This model accounts for the correlation between study level effects induced by multi-arm trials. The model used was based on a random effects logistic regression, with parameters estimated by Markov chain Monte Carlo simulation.

Four network meta-analyses were run for the acute treatment of migraine, each for binary outcomes: headache response at up to 2 hours; freedom from pain at up to 2 hours; sustained headache response at 24 hours and sustained freedom from pain at 24 hours. The log odds ratios were calculated and converted into relative risks for comparison to the direct comparisons. The ranking of interventions was also calculated based on their relative risks compared to the control group. For the acute treatment of migraine, one network was run for change in patient reported migraine days. The change in migraine days for each treatment was calculated, as well as the overall ranking of each treatment based on the effect size compared to placebo.

Data Synthesis for Prognostic Factor Reviews

Odds ratio, relative risks or hazard ratios, with their 95% confidence intervals, from multivariate analyses were extracted from the papers, and standard errors were calculated from the 95% confidence intervals. The log of the effect size with its standard error was entered into the generic inverse variance technique in the Cochrane Review Manager (RevMan5) software (http://ims.cochrane.org/revman). Studies were not combined in a meta-analysis for observational studies.

The quality of studies was assessed and presented in an adapted GRADE profile according to criteria stated in the methodology checklist for prognostic studies in the guidelines manual. Results were reported as ranges.

Data Synthesis for Diagnostic Test Accuracy Review

Evidence for diagnostic data were evaluated by study, using version two of the Quality Assessment of Diagnostic Accuracy Studies checklists (QUADAS-2) (http://www.bris.ac.uk/quadas/quadas-2). For diagnostic test accuracy studies, the following outcomes were reported: sensitivity, specificity, positive predictive value and negative predictive value. In cases where the outcomes were not reported, 2 by 2 tables were constructed from raw data to allow calculation of these accuracy measures. Summary receiver operative characteristic (ROC) curves, would have been generated if appropriate, however there were no data in the diagnostic reviews included in this guideline that could be combined to produce an ROC curve or diagnostic meta-analysis.

Data Synthesis for Qualitative Review

Themes were identified from these studies by two reviewers independently, and then verified jointly. These themes were supplemented with data from surveys where available. Common themes relevant to the question are reported in a narrative in the guideline text.

Appraising the Quality of Evidence by Outcomes

The evidence for outcomes from the included RCT and observational studies were evaluated and presented using an adaptation of the "Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox" developed by the international GRADE working group. The software (GRADEpro) developed by the GRADE working group was used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results. The summary of findings was presented as two separate tables in this guideline. The 'Clinical/Economic Study Characteristics' table includes details of the quality assessment while the 'Clinical /Economic Summary of Findings' table includes pooled outcome data, where appropriate, an absolute measure of intervention effect and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate the sum of the sample size for continuous outcomes. For binary outcomes such as number of people with an adverse event, the event rates (n/N: number of people with events divided by sum of number of people) are shown with percentages. Reporting or publication bias was only taken into consideration in the quality assessment and included in the Clinical Study Characteristics table if it was apparent.

Each outcome was examined separately for the quality elements listed and defined in Table 2 of the full guideline document see "Availability of Companion Documents" field) and each graded using the quality levels listed in Table 3 of the full guideline document (see "Availability of Companion Documents" field). The main criteria considered in the rating of these elements are discussed the tables. Footnotes were used to

describe reasons for grading a quality element as having serious or very serious problems. The ratings for each component were summed to obtain an overall assessment for each outcome.

Grading the Quality of Clinical Evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

1. A quality rating was assigned, based on the study design. Randomized controlled trials (RCTs) start HIGH and observational studies as LOW, uncontrolled case series as LOW or VERY LOW.
2. The rating was then downgraded for the specified criteria: Study limitations, inconsistency, indirectness, imprecision and reporting bias. These criteria are detailed below. Observational studies were upgraded if there was: a large magnitude of effect, dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have 'serious' or 'very serious' risk of bias were rated down -1 or -2 points respectively.
3. The downgraded/upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as HIGH and the overall quality became MODERATE, LOW or VERY LOW if 1, 2 or 3 points were deducted respectively.
4. The reasons or criteria used for downgrading were specified in the footnotes.

The details of criteria used for each of the main quality element are discussed further in sections 2.8.5 to 2.8.8 of the full guideline document (see "Availability of Companion Documents" field).

Evidence of Cost-Effectiveness

Evidence on cost-effectiveness related to the key clinical issues being addressed in the guideline was sought.

The health economist:

- Undertook a systematic review of the economic literature
- Undertook new cost-effectiveness analysis in priority areas

NICE Economic Evidence Profiles

The NICE economic evidence profile has been used to summarise cost and cost-effectiveness estimates. The economic evidence profile shows, for each economic study, an assessment of applicability and methodological quality, with footnotes indicating the reasons for the assessment.

These assessments were made by the health economist using the economic evaluation checklist from The Guidelines Manual (see "Availability of Companion Documents" field). It also shows incremental costs, incremental outcomes (for example, quality-adjusted life-years [QALYs]) and the incremental cost-effectiveness ratio from the primary analysis, as well as information about the assessment of uncertainty in the analysis. See Table 5 in the full guideline document (see the "Availability of Companion Documents" field) for more details.

Where economic studies compare multiple strategies, results are presented in the economic evidence profiles for the pair-wise comparison specified in the review question, irrespective of whether or not that comparison was 'appropriate' within the analysis being reviewed. A comparison is 'appropriate' where an intervention is compared with the next most expensive non-dominated option – a clinical strategy is said to 'dominate' the alternatives when it is both more effective and less costly. Footnotes indicate if a comparison was 'inappropriate' in the analysis.

For particular studies or original models comparing multiple strategies, results are not reported in the standard economic profile but are instead presented at the end of the relevant chapter in a paragraph summarising the study/model as a whole.

Undertaking New Health Economic Analysis

As well as reviewing the published economic literature for each review question, as described above, new economic analysis was undertaken by the Health Economist in priority areas. Priority areas for new health economic analysis were agreed by the GDG after formation of the review questions and consideration of the available health economic evidence.

Additional data for the analysis was identified as required through additional literature searches undertaken by the Health Economist, and discussion with the GDG. Model structure, inputs and assumptions were explained to and agreed by the GDG members during meetings, and they commented on subsequent revisions.

See Appendices J and L (see the "Availability of Companion Documents" field) for details of the health economic analyses undertaken for the guideline.

Cost-Effectiveness Criteria

NICE's report "Social value judgements: principles for the development of NICE guidance" sets out the principles that GDG members should consider when judging whether an intervention offers good value for money.

In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

a. The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
b. The intervention cost less than £20,000 per QALY gained compared with the next best strategy.

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'from evidence to recommendations' section of the relevant chapter with reference to issues regarding the plausibility of the estimate or to the factors set out in the "Social value judgements: principles for the development of NICE guidance."

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Clinical Excellence (NICE) (see the "Availability of Companion Documents" field for the full version of this guidance).

Guideline Development Team

A multidisciplinary Guideline Development Group (GDG) comprising professional group members and consumer representatives of the main stakeholders developed this guideline. The group met every 5-6 weeks during the development of the guideline.

Staff from the NCGC provided methodological support and guidance for the development process. The team working on the guideline included a project manager, systematic reviewers, health economists and information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost effectiveness analysis where appropriate and drafted the guideline in collaboration with the GDG.

Developing Recommendations

Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendices E and F of the full guideline document.
- Summary of clinical and economic evidence and quality (as presented in chapters 4-25 of the full guideline document).
- Forest plots (Appendix G of the full guideline document).
- A description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (Appendices J and L of the full guideline document).

See the "Availability of Companion Documents" field for the full guideline document.

Recommendations were drafted on the basis of the GDG interpretation of the available evidence, taking into account the balance of benefits, harms and costs. When clinical and economic evidence was of poor quality, conflicting or absent, the GDG drafted recommendations based on their expert opinion by informal consensus. The considerations for making consensus based recommendations include the balance between potential harms and benefits, economic or implications compared to the benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues. The consensus recommendations were formed through discussions in the GDG meetings, and voting when there was not clear agreement.

The main considerations specific to each recommendation are outlined in the linking evidence to recommendation section preceding the recommendation section. The guideline recommends some drugs for indications for which they do not have a United Kingdom (UK) marketing authorisation at the date of publication, if there is evidence to support that use. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations. Drug dosages are specified in recommendations where the dosage for that indication is not included in the 'British national formulary'.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Indications for Consideration of Additional Investigation

- There are some costs associated with further investigations and/or referral and with additional examination of the false positives; however the Guideline Development Group (GDG) considered the features listed in the recommendation to be serious and alarming enough to warrant further consideration for investigations and/or referral. The GDG believe these features will help minimise the number of false positives (patients unnecessarily referred for further assessment).
- There are some costs associated with conducting further investigations; however there is a serious risk of fatal illness in a population with compromised immunity if symptoms such as new onset headache are not investigated and appropriate treatment given. The GDG believed that in this population the high risk justifies the cost.
- In a population with a history of malignancy, a new onset headache could be a symptom of brain metastasis. The GDG believed that in this population prompt identification and treatment of brain metastasis justify the cost.

Headache Diaries for the Diagnosis and Management of Primary Headaches and Medication Overuse Headache

Using headache diaries for the diagnosis of the headache type has a cost of £2.80 to £5.64 per person, which includes the cost of the additional time the GP or consultant spent during a consultation in order to evaluate the diary. The additional cost could be offset by the more accurate diagnosis of the correct type of headache, which is important to provide the most cost-effective treatment according to the recommendations in this guideline.

Diagnosis of Primary Headaches and Medication Overuse Headache

- Considering specific characteristics for the diagnosis of headache does not have any economic implications. However diagnosing the correct type of headache is important to provide cost-effective treatments as identified and recommended in this guideline (see Chapters 10-22 in the full guideline document [see the "Availability of Companion Documents" field]).
- The GDG considered the opportunity cost of referring people for further investigation and concluded that given the seriousness of the potential alternative diagnoses in people with rare aura symptoms, making the correct diagnosis justifies the extra cost.

The Role of Imaging in Diagnosis and Management of Primary Headaches

- An original cost-effectiveness analysis based on our clinical review found that imaging strategies have an incremental cost per abnormality detected above £15,000. It is likely that this is an underestimate as the cost of the imaging strategy was calculated based on a mix of magnetic resonance imaging (MRI), computed tomography (CT) and ultrasound, as used in the included clinical studies, while in reality most people would have the most costly MRI. The GDG believed that many of the abnormalities identified would not require specific treatment and change in management, the GDG considered the opportunity cost of finding an abnormality and concluded that extensive imaging for all people presenting with headache would not be cost-effective, while selecting specific populations where the likelihood of finding an abnormality is higher might be more cost-effective.

Information and Support for People with Headache Disorders

- Providing people with relevant information is not considered to generate significant costs and could lead to a more efficient use of resources (for example people making the most efficient use of treatment) and to an improvement in the person's quality of life.
- There might be some costs associated with the time spent by the health care professional in the provision of advice. The GDG considered the potential future cost savings associated with this intervention: less use of medication, fewer visits to health care professional, and they decided this recommendation would lead to health gains and potentially to a net decrease in costs.

Acute Pharmacological Treatment of Migraine With or Without Aura*

- An original cost-effectiveness analysis developed for this guideline showed that triptans are on average more costly than ergots but they are also more effective. At a willingness to pay of £20,000 per quality-adjusted life year (QALY) triptans are more cost-effective than ergots. When the strategies compared in the model are considered altogether (non-steroidal anti-inflammatory drugs [NSAIDs], paracetamol, ergots, triptans, triptans in combination with NSAIDs and triptans in combination with paracetamol), ergots are likely to be the least cost-effective intervention while triptans in combination with NSAID are the most cost-effective intervention.
- The original cost-effectiveness analysis showed that a triptan in combination with NSAID is the most cost-effective treatment for the management of acute migraine. Triptan in combination with paracetamol was the second most cost-effective intervention. They were both more costly than other strategies but they were also more effective.
  In the probabilistic sensitivity analysis, triptan + NSAID was the most cost-effective strategy in about 60% of the simulations while triptan + paracetamol came out the most cost-effective strategy in about 38% of the simulations. While there is some uncertainty when deciding which strategy between the two is the most cost-effective, it is quite certain that both of them are the two most cost-effective options for the acute treatment of migraine.

- Monotherapy with oral triptans, NSAID, and paracetamol were strategies evaluated in an original cost-utility analysis developed for the guideline. Although in the base case analysis triptan + NSAID and triptan + paracetamol are more effective and cost-effective than monotherapies, results might have been driven by the population included in the RCTs for whom monotherapies had already been tried ineffectively.
  Aspirin was not included in the original model developed for the guideline due to the absence of RCT reporting the effectiveness at 24 hours. However based on the acquisition cost, aspirin is less costly than other options and from the clinical evidence it is effective at 2 hours.

  The economic model did not take into account potential adverse events of treatments, therefore these should be considered when deciding the treatment strategy.

Acute Pharmacological Treatment of Cluster Headache

- Oxygen: No economic evidence was identified. The cost of home oxygen service was estimated at £175 per new patient and around £69 per 6-month checkup. However, these figures are not specific to people with cluster headache and costs are expected to be lower due to a better efficient use of resources achieved with the new setup of service provision. Therefore these figures are expected to be an overestimate of the current cost of oxygen. Treatment with oxygen is more costly than other treatments. The GDG thought this cost would be justified by the evidence on effectiveness of oxygen; an effective treatment of cluster headache would lead to some cost savings in terms of fewer emergency visits, fewer medications and improved quality of life for people. Early effective treatment may also reduce work loss due to cluster headaches.
- Triptans: The average costs of subcutaneous triptans and nasal triptans are respectively £21.24 and between £5.90 and £12.16 per episode treatment. The GDG agreed that although subcutaneous triptans cost more than oral triptans, the evidence demonstrates that subcutaneous or nasal triptans are the only preparations which are effective for treatment of cluster headache. The higher acquisition cost would be partly offset by the fewer emergency visits and the fewer medications used.

Prophylactic Treatment of Migraine With or Without Aura*

- An original cost-effectiveness analysis showed that telmisartan is not cost-effective for migraine prophylaxis when compared to no treatment as the incremental cost-efficacy ratio (ICER) is above the £20,000/QALY threshold. When compared to other available strategies (topiramate, propranolol and acupuncture), topiramate is the most cost-effective option, followed by propranolol. When the model was run probabilistically, telmisartan was the most cost-effective strategy in 20.7% of the simulations.
- An economic study directly applicable and with minor limitations, and our original cost-effectiveness analysis showed that topiramate is cost-effective when compared to no treatment as the ICER is below the £20,000/QALY threshold. When compared to other available strategies (telmisartan, propranolol and acupuncture), topiramate is the most cost-effective option, followed by propranolol. When the model was run probabilistically, topiramate was the most cost-effective strategy in 45.2% of the simulations.
- An original cost-effectiveness analysis showed that beta-blockers (propranolol) are cost-effective when compared to no treatment as the ICER is below the £20,000/QALY threshold. When compared to other available strategies (telmisartan, topiramate and acupuncture), topiramate is the most cost-effective option, followed by propranolol. When the model was run probabilistically, propranolol was the most cost-effective strategy in 25.5% of the simulations.

Prophylactic Non-pharmacologic Management of Primary Headache With Acupuncture

- An original cost-effectiveness analysis showed that acupuncture is not cost-effective when compared to no treatment as acupuncture is more

effective but also more costly and the ICER is above the £20,000/QALY threshold. When compared to other available strategies (telmisartan, topiramate and propranolol), topiramate is the most cost-effective option, followed by propranolol. When the model was run probabilistically, acupuncture was the most cost-effective strategy in 6.4% of the simulations. Results are sensitive to the number of acupuncture sessions provided: when the number of sessions is 10 or below, acupuncture is more cost-effective than no treatment.
An economic study partially applicable and with minor limitations showed that acupuncture is cost-effective when compared to no treatment as the ICER is below the £20,000/QALY threshold. In this study the average number of acupuncture sessions was 9. These results are compatible with the findings of our sensitivity analysis on the number of acupuncture visits.

- The original cost-effectiveness model developed for this guideline showed that acupuncture costs on average £273 over 6 months while beta-blockers cost £90. Acupuncture is also less effective than beta-blockers and therefore it is dominated. When all the other strategies compared in the model are considered (oxcarbazepine, valproate, acupuncture, telmisartan, propranolol, topiramate and no treatment), acupuncture is likely to be the least cost-effective intervention.

Management of Medication Overuse Headache

The GDG discussed the economic implications of withdrawal strategies compared to prophylactic treatment. There are higher medication costs in the prophylactic treatment strategy due to the prophylactic treatment itself but also to the more frequent acute medication use; however inpatient and outpatient detoxification programmes are also associated with costs. The GDG considered advising people to withdraw the overused medication as the most cost-effective option. However, when this proves unsuccessful, given the evidence on its clinical benefit, the adjunct of prophylactic treatment was considered cost-effective.

*See Appendices J and L in the full guideline document (see the "Availability of Companion Documents: field) for details of the health economic network meta-analyses for acute and prophylactic pharmacologic management of migraine.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was validated through two consultations.

1. The first draft of the guideline (the full guideline, National Institute for Health and Clinical Excellence [NICE] guideline, and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG)
2. The final consultation draft of the full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting each recommendation is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Accurate diagnosis and more effective management of primary headache and medication overuse headache

Potential Harms

- Adverse effects of acupuncture, including a small risk of pneumothorax
- Cardiac conduction problems from verapamil
- Development of medication overuse headache when prescribing acute treatment for tension type headache
- Gastric ulceration, reduce renal function or anaphylactic reaction from non-steroidal anti-inflammatory drugs (NSAIDs)
- Extra pyramidal side effects from anti-emetics
- Transient worsening before the improvement with subcutaneous triptan administration for acute cluster headache

Women of Child-Bearing Potential

- Topiramate may reduce the reliability of combined hormonal contraception at doses greater than 200mg/day.
- The risk of medication overuse headache should be considered when triptans are used for prophylaxis of menstrual migraine.

Refer to "Trade off between clinical benefits and harms" for each recommendation in the full version of the original guideline document (see the "Availability of Companion Documents" field) for a more detailed discussion of benefits and harms.

Contraindications

Contraindications

- Oxygen is not advised in people with chronic obstructive pulmonary disease (COPD) and it should be used with caution in people with respiratory disease.
- Bearing in mind that topiramate is a teratogen and the potentially serious consequences of a pregnancy, the Guideline Development Group (GDG) recommends that women of child-bearing potential using topiramate be advised to use a reliable contraceptive method such as medroxyprogesterone acetate depot injection or an intrauterine method (coil or Mirena®) as their metabolism is suggested to be unaffected by topiramate.
- The current advice from the World Health Organization (WHO) in Medical Eligibility criteria for contraceptive use recommends that oral contraceptive pill should not be used in women with aura at any age.
- Because of an association with Reye's syndrome, preparations containing aspirin should not be offered to people aged under 16 years.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of National Institute for Health and Clinical Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- The guideline assumes that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.
- Treatment and care should take into account people's needs and preferences. People with headaches should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If people do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent and the code of practice that accompanies the Mental Capacity Act. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.
- If the person is under 16, healthcare professionals should follow the guidelines in Seeking consent: working with children .

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Clinical Excellence (NICE) has developed tools to help organisations implement this guidance. These are available on the NICE Web site (see also the "Availability of Companion Documents" field).

Implementation Tools

Audit Criteria/Indicators

Chart Documentation/Checklists/Forms

Clinical Algorithm

Patient Resources

Resources

Staff Training/Competency Material

Wall Poster

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Clinical Guideline Centre. Headaches: diagnosis and management of headaches in young people and adults. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Sep. 38 p. (Clinical guideline; no. 150).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Sep

Guideline Developer(s)

National Clinical Guideline Centre - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Clinical Excellence (NICE)

Guideline Committee

Guideline Development Group (GDG)

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members declared interests including consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared arising conflicts of interest, which were also recorded. Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix B of the full guideline document (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Clinical Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Diagnosis and management of headaches in young people and adults. Full guideline. London (UK): National Institute for Clinical Excellence (NICE); 2012 Sep. 360 p. (Clinical guideline; no. 150). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Diagnosis and management of headaches in young people and adults. Appendices. London (UK): National Institute for Clinical Excellence (NICE); 2012 Sep. 630 p. (Clinical guideline; no. 150). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Combination therapy for first-line treatment of acute migraine. Academic detailing aid. London (UK): National Institute for Clinical Excellence (NICE); 2012 Sep. 4 p. (Clinical guideline; no. 150). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Headaches. Baseline assessment tool. London (UK): National Institute for Clinical Excellence (NICE); 2012 Sep. (Clinical guideline; no. 150). Electronic copies: Available from NICE Web site.
- Headaches: management of cluster headache. Clinical audit tool. London (UK): National Institute for Clinical Excellence (NICE); 2012 Sep. 8 p. (Clinical guideline; no. 150). Electronic copies: Available from the NICE Web site.
- Headaches. Clinical case scenarios. London (UK): National Institute for Clinical Excellence (NICE); 2012 Sep. (Clinical guideline; no. 150). Electronic copies: Available in Portable Document Format (PDF) and PowerPoint format from the NICE Web site.
- Headaches. Costing report. London (UK): National Institute for Clinical Excellence (NICE); 2012 Sep. 19 p. (Clinical guideline; no. 150). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Headaches. Costing template. London (UK): National Institute for Clinical Excellence (NICE); 2012 Sep. (Clinical guideline; no. 150). Electronic copies: Available from NICE Web site.
- Diagnosis of tension-type headache, migraine and cluster headache. Diagnosis poster. London (UK): National Institute for Clinical Excellence (NICE); 2012 Sep. 1 p. (Clinical guideline; no. 150). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- NICE Pathways. Headaches: Overview. London (UK): National Institute for Clinical Excellence (NICE); 2012 Jun. Electronic copies: Available from the NICE Web site.
- The guidelines manual 2009. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Jan. Electronic copies: Available from the NICE Archive Web site.

Patient Resources

The following is available:

- Headaches. Information for the public. London: National Institute for Health and Clinical Excellence (NICE); 2012 Sep. 15 p. Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This summary was completed by ECRI Institute on October 26, 2012. This summary was updated by ECRI Institute on October 28, 2013 following the U.S. Food and Drug Administration advisory on Acetaminophen. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs).

The National Institute for Health and Clinical Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include

summaries of their clinical guidelines with the intention of disseminating and facilitating the implementation of that guidance. NICE has not yet verified this content to confirm that it accurately reflects that original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE clinical guidelines are prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk .

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